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**WO 2004/010987 A3**

(54) Title: USE OF S1P RECEPTOR AGONISTS IN HEART DISEASES

(57) Abstract: The invention relates to the use of a sphingosine-1-phosphate receptor agonist in the treatment of heart diseases.

## INTERNATIONAL SEARCH REPORT

International Application No. 52129  
PCT/EP 03/08085A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61K31/13 A61K31/137 A61K45/00  
A61P9/10A61P9/04 A61P9/06  
14 JAN 2005

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, PAJ, EMBASE, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KARLINER J S: "Lysophospholipids and the cardiovascular system" BIOCHIMICA ET BIOPHYSICA ACTA, ELSEVIER,, vol. 1582, no. 1-3, 23 May 2002 (2002-05-23), pages 216-221, XP004366543 page 219, left-hand column, paragraph 2 - right-hand column, paragraph 4 -----	1-4
X	PYNE S ET AL: "SPINGOSINE 1-PHOSPHATE SIGNALLING VIA THE ENDOTHELIAL DIFFERENTIATION GENE FAMILY OF G-PROTEIN-COUPLED RECEPTORS" PHARMACOLOGY AND THERAPEUTICS, ELSEVIER, GB, vol. 88, 2000, pages 115-131, XP002254562 ISSN: 0163-7258 page 127, left-hand column, paragraph 1-3 ----- -/-	1-4

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

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19.02.2004

Name and mailing address of the ISA

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Young, A

## INTERNATIONAL SEARCH REPORT

Int'l Application No  
PCT/EP 03/08085

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 004 565 A (CHIBA KENJI ET AL) 21 December 1999 (1999-12-21) column 3, line 20 - column 5, line 7 column 8, line 15 -----	1-4,7
X	LILIOOM KAROLY ET AL: "Sphingosylphosphocholine is a naturally occurring lipid mediator in blood plasma: A possible role in regulating cardiac function via sphingolipid receptors" BIOCHEMICAL JOURNAL, vol. 355, no. 1, 1 April 2001 (2001-04-01), pages 189-197, XP002258995 ISSN: 0264-6021 page 196, left-hand column, paragraph 4 - right-hand column, paragraph 1 -----	1-4
X	EP 0 627 406 A (YOSHITOMI PHARMACEUTICAL) 7 December 1994 (1994-12-07) cited in the application the whole document -----	1-4,7
A	CLELAND J G F ET AL: "WHAT IS THE OPTIMAL MEDICAL MANAGEMENT OF ISCHAEMIC HEART FAILURE?" BRITISH MEDICAL BULLETIN, CHURCHILL LIVINGSTONE, LONDON, GB, vol. 59, 2001, pages 135-148, XP008017622 ISSN: 0007-1420 the whole document -----	5,6
A	LYNCH K R: "Lysophospholipid receptor nomenclature" BIOCHIMICA ET BIOPHYSICA ACTA, ELSEVIER, vol. 1582, no. 1-3, 23 May 2002 (2002-05-23), pages 70-71, XP004366523 the whole document -----	1-7
X,P	WO 03/020313 A (ONO PHARMACEUTICAL CO ;NAKADE SHINJI (JP); SUZUKI HIDEHIRO (JP)) 13 March 2003 (2003-03-13) abstract -----	1-7

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 03/08085

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  

Although claims 4,6 and 7 (part) are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  

see FURTHER INFORMATION sheet PCT/ISA/210
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple Inventions in this International application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the Invention first mentioned in the claims; it is covered by claims Nos.:  

1-7 (part)

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: -

Present claims 1-6 relate to a product/compound/method defined by reference to a desirable characteristic or property, namely S1P receptor agonist.

The claims cover all products/compounds/methods having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products/compounds/methods. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product/compound/method/apparatus by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the products/compounds/methods as disclosed in claim 7 (i.e. formula I for invention 1).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-7 (part)

Use, a pharmaceutical composition, a pharmaceutical combination or a method according to claims 1-6 wherein the S1P receptor agonist is selected from a compound of formula I.

---

2. claims: Claims 1-7 (part)

Use, a pharmaceutical composition, a pharmaceutical combination or a method according to claim 1-6 wherein the S1P receptor agonist is selected from a compound of formula II.

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3. claims: Claims 1-7 (part)

Use, a pharmaceutical composition, a pharmaceutical combination or a method according to claims 1-6 wherein the S1P receptor agonist is selected from a compound of formula III.

---

4. claims: Claims 1-7 (part)

Use, a pharmaceutical composition, a pharmaceutical combination or a method according to claims 1-6 wherein the S1P receptor agonist is selected from a compound of formula IVa or IVb.

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5. claims: Claims 1-7 (part)

Use, a pharmaceutical composition, a pharmaceutical combination or a method according to claims 1-6 wherein the S1P receptor agonist is selected from a compound of formula V.

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6. claims: Claims 1-7 (part)

Use, a pharmaceutical composition, a pharmaceutical combination or a method according to claims 1-6 wherein the S1P receptor agonist is selected from a compound of formula VI.

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## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/08085

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
US 6004565	A	21-12-1999	JP US	11080026 A 2002102279 A1		23-03-1999 01-08-2002
EP 0627406	A	07-12-1994	CA DE DE DK EP HK US AT CY ES WO JP KR US US	2126337 A1 69321823 D1 69321823 T2 627406 T3 0627406 A1 1013281 A1 5604229 A 172711 T 2215 A 2126658 T3 9408943 A1 2579602 B2 155015 B1 5719176 A 5952316 A		28-04-1994 03-12-1998 02-06-1999 12-07-1999 07-12-1994 02-06-2000 18-02-1997 15-11-1998 18-04-2003 01-04-1999 28-04-1994 05-02-1997 01-12-1998 17-02-1998 14-09-1999
WO 03020313	A	13-03-2003	WO	03020313 A1		13-03-2003

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(EO)

U.S. APPL. NO.

**10/521297**

INTERNATIONAL APPL.

*EPA003/008085*

APPLICATION FILED BY: 20 MOS. OR 30 MOS. SCREENED BY

INTERNATIONAL APPLICATION PAPERS IN THE APPLICATION FILE:

- International application
- Article 19 amendments
- Priority Document(s) No.
- Request Form PCT/RO/101
- PCT/IB/302
- PCT/IB/304
- PCT/IB/306
- PCT/IB/308
- PCT/IB/331
- OTHER PCT/IB/
- PCT/IPEA/409 also 416

- A09 annexes to IPER
- PCT/ISA/210 (Search report)
- Search report References
- Other Papers filed

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- Used the IB copy of the IA
- Description
- Claims
- Drawings
- Foreign Language in drawing
- Article 19 Amendments
- Amendment used in application
- Article 34 Amendment
- Amendment used in application
- DNA
- 1194 transaction done

- Preliminary Amendment(s) filed 14 Jan 05
- second submission
- Information Disclosure Statement 17 Aug 05
- second submission
- Assignment
- Forward to Assignment Branch
- Substitute Specification
- Small Entity Statement
- type
- Oath/Declaration (date submitted )
- Not executed
- Executed
- Power of Attorney
- Change of Address

USC Receipt of Request (PTO - 1399 Transmittal Letter)  
to Acceptable oath/declaration received

14 Jan 05

2(e) Date

to complete 35 USC 371 requirements met

DATE NOTICE COMPLETED

4/16/05

- IEO 903 Notice of Acceptance
- IEO 905 Notice of Missing Requirements
- IEO 917 Notice of A defective oath or declaration
- IEO 916 Notice of defective response

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